## REMARKS

Attached hereto is a marked-up version of the changes made to the claims by the above amendment. The attached page is captioned **"Version with markings to show changes made."**

Claim 1 has been amended to include the limitations of claims 8 and 9 without acquiescence to positions set forth in the Action. Similarly, claim 3 has been amended to include the limitations of claims 16 and 17 without acquiescence to positions set forth in the Action. Claims 1 and 3 have also been amended to recite "a set of oligopeptides", which is supported at least in the paragraph bridging pages 6 and 7 of the application; on page 7, lines 12-15; and on page 8, lines 11-14.

These amendments have been made for reasons related to business considerations and currently contemplated embodiments of the invention rather than in acquiescence to any position set forth in the Office Action. Applicants reserve the right to pursue the claims as previously filed in a continuing application.

Claims 8 and 9 have been amended to contain the subject matter of previous claim 9. Similarly, claims 16 and 17 have been amended to contain the subject matter of previous claim 17.

Claim 14 has been amended to correct a clerical error in its claim dependency.

No new matter has been introduced, and entry of the amendments is respectfully requested.

***Interview on December 17, 2002***

Applicants thank Examiner T. Wessendorf for the courtesy of a telephonic interview on December 17, 2002. The discussion included all of the issues contained in the Office Action mailed November 26, 2002 as well as Applicants' view that finality was premature in the instant application. The Examiner's position with respect to particular issues was discussed in detail, and Applicants submit the instant response in an effort to advance prosecution in the instant application.

***Premature finality***

Applicants renew their assertion that finality of the instant Office Action is premature because claims 13-18 should have been examined on their merits in Paper No. 21 (Office Action

mailed May 20, 2002). That Action was not made "final", and improperly withdrew claims 13-18 as "directed to a non-elected invention" when the claims were in fact dependent from pending claim 3.

While Applicants thank Examiner Wessendorf for recognizing that claims 13-18 are not directed to subject matter subject to restriction, Applicants note that the instant Office Action has examined and rejected claims 13-18 for the first time. Applicants believe, however, that *these claims should be treated in a "non-final" manner as in Paper No. 21.* To do otherwise is to deny Applicants the opportunity to have addressed the rejection of the claims in the Response to Paper No. 21. Stated differently, Applicants have had no opportunity to address the rejections of claims 13-18 under "non-final" conditions.

Therefore, Applicants respectfully submit that finality in the instant Action is premature and should be withdrawn.

***Rejections under 35 U.S.C. § 112***

Claims 1, 3, 5-10 and 13-20 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly non-enabled. Applicants have carefully reviewed the statement of the rejection and considered the Examiner's position as discussed during the telephonic interview of December 17, 2002.

The position set forth in the instant rejection appears to be based upon the allegation that all proteins bind to all other proteins and that recitation of particular peptides on a replicable display package is necessary for enablement of the instant invention.

Applicants note that as discussed during the telephonic interview of December 17, 2002, the present invention may be viewed in light of existing knowledge concerning phage display technology in general. An example of such knowledge is in USP 5,837,500, where claim 1 is as follows:

> "A method of obtaining a nuclecic acid encoding a proteinaceous binding domain that binds a predetermined target material comprising:
>
> a) preparing a variegated population of filamentous phage, each phage including a nucleic acid construct coding for a chimeric potential binding protein, each said construct comprising DNA encoding (i) **a potential binding domain** which is a mutant of a

predetermined parental binding domain, and (ii) an outer surface transport signs for obtaining the display of the potential binding domain on the outer surface of the phage, wherein said variegated population of phage collectively display a plurality of different potential binding domains, the differentiation among said plurality of different potential binding domains occuring through the at least partially random variation of one or more predetermined amino acid position of said parental binding domain to randomly obtain at each said position an amino belonging to a predetermined set of two or more amino acids, the amino acids of said set occuring at said position in predetermined expected proportions, said phage being separable on the basis of the potential binding domains displayed thereon;

b) causing the expression of said potential proteins and the display of said potential binding domains on the outer surface of said phage;

c) contacting said phage with the predetermined target material such that said potential binding domains and the target material interact;

**separating phage displaying a potential binding domain that binds the target material from phage that do not so bind**, and

e) recovering at least one phage displaying on its outer surface a chimeric binding protein comprising a successful binding domain (SBD) which bound said target, said phage enclosing SBD-encoding nucleic acid, and amplifying said SBD-encoding nucleic acid in vivo or in vitro." (emphasis added)

A copy of the front page and claims from the patent are attached to this response. As noted by the bolded text above, the allegation that all proteins bind all other proteins such that the recitation of specific proteins is necessary for the practice of phage display is at odds with the language of the above patented claim, where even closely related protein binding domains expressed on phage may be identified as either binding, or not binding, a target material. If a skilled artisan could practice such methods at the time of the patent without undue experimentation, how could there now be undue experimentation to practice the instantly claimed methods? Therefore, Applicants respectfully submit that recitation of particular peptides for display is ***not*** necessary for the instant claims to be enabled by the instant specification.

Accordingly, no undue experimentation is required to practice the invention as claimed prior to the above amendments to claims 1 and 3.

Nevertheless, and in an effort to advance prosecution in this case after multiple Office Actions, Applicants have amended the claims to recite particular peptides for display as previously recited in claims 8, 9, 16, and 17. Applicants believe that these amendments address the Examiner's view and submit that this rejection may be properly withdrawn.

Claims 3, 19 and 20 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite. Applicants have carefully reviewed the statement of the rejection and believe that the claims are definite for the following reasons.

With respect to claims 19 and 20, Applicants again note that support for the claims is provided at least on page 7, lines 30-33 of the specification. This passage relates to a "target protein" as opposed to a "proteinaceous target" or "proteinaceous antigen". Applicants point out that the scope of "proteinaceous target" or "proteinaceous antigen" includes 1) targets and antigens that are composed of both a protein component and a non-protein component as well as 2) targets and antigens that are composed only of protein. An example of 1) is a ribosomal complex, which has both protein and nucleic acid components. An example of 2) is bovine ribonuclease, which is a single polypeptide chain. Claims 19 and 20 are intended to emphasize this point by being directed to situations corresponding to 2) as described above.

Claims 19 and 20 generate no confusion with respect to the recitation of "oligopeptides derived from" a "proteinaceous target" or "proteinaceous antigen" as recited in claims 1 and 3 because it is clear that such oligopeptides would be derived from the protein component of the target or antigen in either of case 1) or 2) above. Therefore, the claims are definite, and withdrawal of the rejection is respectfully requested.

With respect to claim 3, Applicants are confused. The statement of the rejection refers to the rejection of claim 3 on "page 3, paragraph B of the last Office Action" (Paper No. 21). Applicants are unable to locate a "paragraph B" on page 3 of that Action. Additionally, paragraph no. 9 on page 3 of that action only rejects "[c]laim 1 (and dependent claims)" under this statute. Claim 3 was not dependent from claim 1, and so Applicants were unaware of a rejection of the claim under 35 U.S.C. § 112. Therefore, and contrary to the allegation in the instant Action, no acquiescence to any rejection occurred.

On review of page 3 in Paper No. 21, Applicants believe that the rejection was actually for the same reasons as addressed in pages 4 and 5 of Applicants last response, which further demonstrates that no acquiescence occurred. Applicants also believe that the alleged indefiniteness is addressed by the arguments made above with respect to the alleged non-enablement of the invention. Accordingly, the rejection of claim 3 may also be properly withdrawn.

***Prior art rejection under 35 U.S.C. § 102(b)***

Claims 1 and 3 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Barsomian et al. (WO 95/15982). Applicants have carefully reviewed the statement of the rejection and the cited prior art and traverse for the following reasons.

Applicants respectfully note that the instant rejection failed to present a *prima facie* case of anticipation of claim 1 as originally filed because Barsomian et al. do not disclose the act of directly synthesizing oligopeptides on a solid phase. Instead, Barsomian et al. describe the immobilization of a single "target antigen" on an insoluble carrier (see page 29, line 36, to page 30, line 2). This is not the same as synthesizing multiple *oligopeptides* on a solid phase as previously recited in the claims.

Applicants strongly disagree with the instant Action's apparent assertion of an "inherent" teaching of synthesis by Barsomian et al. because the claims are directed to a method comprising the physical act of synthesis. Because Barsomian et al. do not teach such an act and instead teach the immobilization of a whole antigen, no anticipation, inherent or otherwise, exists. Moreover, and even assuming for the purposes of argument that the act of immobilizing a whole antigen was inherently the same as synthesizing a polypeptide on a solid phase, such immobilizing would still not be of **more than one oligopeptide** derived from a proteinaceous target or antigen as recited in the claims. Therefore, no claim amendment was necessary to obviate this rejection, and the instant rejection should be withdrawn based on the above discussion.

To further emphasis the distinction between the claimed invention and Barsomian et al., however, claims 1 and 3 have been amended to recite that "a set" of oligopeptides derived from a proteinaceous target or antigen is synthesized on a solid phase. This reflects use of alternative

language directed to the same plurality of oligopeptides as previously recited in the claims. No change in claim scope has occurred.

The immobilization of a single "target antigen" as disclosed by Barsomian et al. is not the same as, nor does it suggest, synthesizing a set of oligopeptides as encompassed by the claims. Therefore, no issue of anticipation is present, and the instant rejection may be withdrawn.

Claims 1, 3, 5-10 and 13-20 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Kruif et al. (J. Mol. Biol.). Applicants have carefully reviewed the statement of the rejection and the cited prior art and traverse for the following reasons.

As an initial matter, the previous rejection in light of Kruif et al. on pages 7 and 8 of Paper No. 21 ends with the statement that "the Kruif et al. reference suggests the synthesizing of one or more oligopeptide 'derived from a protein target' on a substrate for screening a phage library peptide ligand" (underlining in the original). Applicants interpreted this as acknowledgement by the previous Examiner of Kruif et al. failing to actually **teach** the limitation in claims 1 and 3 and so interpreted the rejection as based upon obviousness rather than anticipation.

In light of the emphasis in the instant Action of the rejection being based upon anticipation and the apparent treatment of immobilized antigen as equivalent to oligopeptides synthesized on a solid phase, Applicants respectfully submit that no *prima facie* case of anticipation has been presented essentially for the same reasons as discussed above with respect to Barsomian et al.

Again, Applicants note that no anticipation of claim 1 as originally filed is present because Kruif et al. do not disclose the act of synthesizing oligopeptides on a solid phase. Instead, Kruif et al. describe the use of "antigen-coated immunotubes" (see page 103, left column, first full paragraph, first sentence). No oligopeptides derived from a single proteinaceous target or antigen are disclosed. Therefore, no synthesizing of multiple *oligopeptides* on a solid phase as previously recited in the claims is disclosed, literally or inherently. Therefore, no claim amendment was necessary to obviate this rejection, and the instant rejection should be withdrawn on this basis alone.

As for the instant Action's questions concerning the terms "solid phase bound antigens" and "antigens which are synthesized on solid phase", Applicants respectfully point out that the

first term does not require an actual act of synthesis of a polypeptide antigen on the solid phase while the second term does. Claims 1 and 3 both positively recite the limitation that an act of synthesis of oligopeptides on a solid phase is necessary to be within the scope of the claims. Applicants do not believe that mere immobilization of a single antigen is equivalent to the synthesis of multiple oligopeptides. Immobilization is not the same as synthesis, and a single antigen is not the same as oligopeptides.

As noted above, the distinction between the claimed invention and Kruif et al. has been further emphasized by amending claims 1 and 3 to recite that "a set" of oligopeptides derived from a proteinaceous target or antigen is synthesized on a solid phase. No change in claim scope has occurred by the use of this alternative language directed to the same plurality of oligopeptides as previously recited in the claims.

The immobilization of an "antigen" as disclosed by Kruif et al. is not the same as, nor does it suggest, synthesizing a set of oligopeptides as encompassed by the claims. Therefore, no issue of anticipation is present, and the instant rejection may be withdrawn.

***Conclusion***

Applicants believe that all issues of record have been addressed and that the claims are allowable. They respectfully urge early indication to that effect. The Examiner is encouraged to contact the undersigned to discuss any residual matters to expedite prosecution of the instant application.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 313632000600.

Respectfully submitted,

Dated: January 24, 2003 By: _____

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## VERSION WITH MARKINGS TO SHOW CHANGES MADE

**In the Claims:**

Kindly amend the claims as follows:

1. (twice amended) A method for identifying a peptide capable of binding to a proteinaceous target comprising

displaying the peptide on the surface of a replicable display package,

synthesizing a set of oligopeptides derived from the proteinaceous target on a solid phase,

contacting the binding peptide on the surface of said package with the oligopeptides on said solid phase, and

identifying whether binding occurs,

wherein the displayed peptide on the surface of a replicable display package is an immunoglobulin heavy chain, an immunoglobulin light chain, a heavy-light chain pair, a single chain antibody fragment, VH, a VL, a Fab, a Fv, an scFv or a di-sulfide-bridged Fv.

3. (twice amended) A method for distinguishing between peptides capable of binding to a proteinaceous antigen and peptides not having that capability comprising

displaying candidate peptides on the surfaces of replicable display packages,

synthesizing a set of oligopeptides derived from the proteinaceous antigen on a solid phase,

contacting the candidate peptides on the surfaces of said packages with the oligopeptides on said solid phase to permit binding by said candidate peptides, and

washing the solid phase to remove unbound display packages,

wherein the displayed candidate peptides are immunoglobulin heavy chains, immunoglobulin light chains, heavy-light chain pairs, single chain antibody fragments, VH domains, VL domains, Fab domains, Fv domains, scFv domains or di-sulfide-bridged Fv domains.

8. (twice amended) A method according to claim 1, whereby the displayed peptide is [~~an immunoglobulin heavy chain, an immunoglobulin light chain, a heavy-light chain pair, a VH, a VL, a Fab, a Fv, an scFv or a di-sulfide-bridged Fv~~] a single chain antibody fragment.

9. (twice amended) A method according to claim 1 whereby the displayed peptide is [~~a single chain antibody fragment or~~] an ScFv.

14. (amended) A method according to claim [~~13~~] 3, whereby the replicable display packages are bacteria, yeast or spores of a microorganism.

16. (amended) A method according to claim 3, whereby the candidate peptides are [~~immunoglobulin heavy chains, immunoglobulin light chains, heavy-light chain pairs, VH domains, VL domains, Fab domains, Fv domains, scFv domains or di-sulfide-bridged Fv domains~~] single chain antibody fragments.

17. (amended) A method according to claim 3 whereby the candidate peptides are [~~single chain antibody fragments or~~] ScFv domains.